

REMARKS

The claims have been amended in order to clarify the nature of the subject matter claimed and in order to address the rejections for lack of clarity and under 35 U.S.C. § 112, first paragraph.

First, claims which include intramolecular linkers (RAL) have been segregated from claims that refer to intermolecular linkers (ERL). Claim 23 now exclusively concerns RAL, and the aspect of claim 23 which formerly dealt the ERL appears in new claim 45. The sources of RAL and ERL have been defined in these claims consistent with the explanation in the specification. Claim 26, which identifies specific sequences for ERL, has been canceled and replaced by claim 46, dependent on claim 45 for good order. New claims 47-58 are identical to previously pending claims 28-39 but depend on claim 45 rather than claim 23. It should be apparent that no new matter has been introduced and entry of the amendment is respectfully requested.

Applicants will address the points made in the Office action in turn.

Paragraph 5 of the Office action is actually an objection to the specification indicating that the specification is confusing because of assertedly conflicting definitions of modules. It is believed that the two definitions focused on by the Office are not actually conflicting; rather, they reflect the rather loose terminology generally employed in the art. As explained in the specification, what is often called a "module" extends to the N-terminal or the C-terminal ends of an open reading frame and as to each module, may include a portion of an intramolecular linker if more than one catalytic domain is contained in the same reading frame. Perhaps the enclosed figure from U.S. patent 6,391,594 will be of some help. As seen, even in this figure, there is some ambiguity. As shown, in DEBS1, the catalytic domains are spread out on a scaffold, the N- and C-terminal ends of which are evidently missing in the upper diagram but are shown in the generic module in the lower diagram in

the same figure. The drawing of DEBS1 should actually have a straight line extension from the leftmost AT and from the rightmost ACP which are the extending portions that are part of intermolecular linkers. The intramolecular linkers are, however, shown and, for example, what is shown as module 1 includes some sequence that extends beyond the most upstream KS and the most downstream ACP. Because the linkers in the invention are indeed these “extra sequences” a precise definition was provided in the application for reference when the word is used in the claims. Thus, as set forth in the claims, the definition on page 6 is what is intended since it is recognized that there are remaining sequences in the open reading frame that are immediately upstream from the KS domain and immediately downstream from the ACP. These upstream and downstream sequences are segments of the linker sequences that are the subject of the application. If two adjacent modules are in the same reading frame, the sequence at the C-terminus of the upstream ACP will connect to the N-terminus of the downstream KS and constitute the RAL as the Office recognizes. If the adjacent modules are in different but adjacent open reading frames, the extra sequence at the C-terminus of the ACP preceding the amino acid sequence at the N-terminus of the next sequential module KS together will constitute an ERL or inter-molecular linker.

It is emphasized that those portions of the modules that are limited to the KS; AT; β keto-modifying (BKM); and ACP domains are intended so that the linkers can be used to manipulate the “business” portion of the module as described.

With respect to Example 2, since the diketide is not being passed from one module to the other, but rather simply loaded onto the module, only the N-terminal portion of the ERL is required. The claims as presently constructed do not include this embodiment. With respect to Example 4, module 5 is cut off at the N-terminus of the KS catalytic domain and coupled to the amino acid

sequence that is ordinarily present between the C-terminus of the ACP of module 1 and the N-terminus KS of module 2.

If this explanation is unclear, a telephone call to the undersigned is respectfully requested. Perhaps it is easier to explain this on an interactive basis.

In paragraph 8 of the Office action, the indefiniteness rejection with regard to RAL is withdrawn, which applicants appreciate.

As kindly suggested by the Office, in order to propose claims that are clearly free of this rejection, claim 23 and its dependent claims 25 and 28-39 are now limited to RAL and new claims 44-58 are separately constructed to claim ERL.

Paragraph 9 of the Office action maintains the rejection of all pending claims with regard to indefiniteness of the term “inter-molecular linkers (ERL).” As stated above, the aspect of the invention related to ERL has been moved to a different set of claims, so claims 23, 25 and 28-39 are free of this rejection. Claim 45 now contains a definition of ERL. In order for an inter-molecular linker to function, the matching “C-terminal ERL” in the module that materially precedes the “N-terminal ERL” immediately following it must be employed in the context where a polyketide chain is being passed between sequential modules. It does not matter whether the “business” portion of the modules are in different open reading frames in a native PKS or whether they are in the same reading frame. An ERL (a complete ERL with both the C-terminal ERL and its matching N-terminal ERL) can be used to link any two modules where a growing polyketide chain is passed from one module to the other. Again, the “modules” are only the portions that contain the sequences represented as KS-AT-BKM-ACP domains and do not include the amino acid sequences that form the linkers between the C-terminus of an ACP with the N-terminus of the KS of the next

module (again, regardless of whether the upstream and downstream modules are or are not in the same reading frame). It is believed that claim 45 as currently worded makes this clear.

As noted above, in response to the citation of Example 2, the embodiment reflected in that example does not appear in the present set of claims. Claim 45 merely deals with the situation where there are two adjacent modules which must pass the growing polyketide chain from a first module to the second. In this instance, both a C-terminal ERL and its matching N-terminal ERL must be included between the two adjacent modules.

With respect to the rejection of all claims under 35 U.S.C. § 112, first paragraph, the amendments to the claims have defined the RAL's and ERL's in as clear structural terms as permitted by Mother Nature and the subject matter of the invention. (It is not clear why claim 25 was included in this rejection as the structural limitations of the RAL are set forth in that claim.) As described in previous submissions, one of ordinary skill would readily be able to identify these regions in any given PKS, given the guidance in the specification and the ordinary skill of the art. Applicants appreciate the helpful suggestion made by the Examiner to use "product-by-process" language to identify the RAL and ERL sequences. It is believed that this has effectively been done by defining these sequences as those intermediate between the consensus sequences in the amended claims.

With respect to the portion of the rejection set forth in paragraph 11, this appears to be an objection to the assertedly waffling nature of the term "is facilitated." Thus, it appears this is an issue of claim wording, and it is believed that the amendment to the claims makes it clear that the nascent polypeptide chain is actually passed from the first module to the second.

CONCLUSION

The claims have been amended to clarify the nature of the invention and to define the RAL and ERL elements structurally. It is believed that the claims as amended are responsive to the outstanding rejections and that all pending claims, claims 23, 25, 28-39 and 45-58, are in a position for allowance. Passage of these claims to issue is respectfully requested.

If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 300622004600.

Respectfully submitted,

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